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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/919,102	07/31/2001	Howard Fein	HOFE / 02	2446

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EXAMINER	
WITZ, JEAN C	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 09/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/919,102	FEIN, HOWARD	
	Examiner	Art Unit	
	Jean C. Witz	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5,8,9,24,25,30,31,34,35,37-40 and 43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,5,8,9,24,25,30,31,34,35,37-40 and 43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 3, 2005 has been entered.

Response to Arguments

2. Insofar as Applicant's arguments filed August 18, 2005 apply to the new ground(s) of rejection, they have been fully considered but they have not been found to be persuasive for the reasons set forth below.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-2, 4-5, 8-9, 24-25, 30-31, 34-35, 37-40 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over the disclosure of SU1685448 in view of U.S. Patent to Rawlings et al., U.S. Patent 4,112,121 to Tenta, U.S. Patent 5,411,741 to Zaias and non-patent literature reference to Burbach, Dermatologica 118: 379-391 (1959).

The claims recite methods for treating a patient having a condition affecting at least one layer of the skin comprising administering a formulation consisting essentially of at least one hydrolase in an amount and for a duration effective to regulate removal of said layer and treat said condition. In response to an election of species requirement made by the Examiner in the office action dated Dec. 4, 2003, Applicant elected the condition of seborrheic keratosis as the condition and trypsin as the hydrolase.

Foreign patent SU1685448 discloses a method of treating seborrheic keratopapillomata (a synonym for seborrheic keratosis) by administering topically to the lesion a composition containing DMSO, theophylline, trypsin, lanolin and sunflower oil. When applied to the skin for a period of 1-2 days and covered with an occlusive dressing, within 3 weeks of the commencement of the treatment, a complete recovery was seen.

As indicated above, the formulation that is used in the practice of the claimed method is recited as "consisting essentially of trypsin". Per the MPEP at 2111.03, the transitional phrase "consisting essentially of" limits the scope of a claim to the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention. In re Herz, 537 F.2d 549, 551-52, 190 USPQ 461, 463 (CCPA 1976) (emphasis in original). See also Atlas Powder v. E.I. duPont de Nemours & Co., 750 F.2d 1569, 224 USPQ 409 (Fed. Cir. 1984); In re Janakirama-Rao, 317 F.2d 951, 137 USPQ 893 (CCPA 1963); Water Technologies Corp. vs. Calco, Ltd., 850 F.2d 660, 7 USPQ2d 1097 (Fed. Cir. 1988).

For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355 ("PPG could have defined the scope of the phrase consisting essentially of' for purposes of its patent by making clear in its specification what it regarded as constituting a material change in the basic and novel characteristics of the invention."). Applicant states, at page 18 of the specification, that "[t]he composition containing an enzyme or mixture of enzymes may also contain other compounds that have desirable therapeutic, cosmetic, and/or aesthetic properties, that either do not affect or only minimally affect the activity of the enzyme." If an applicant contends that additional materials in the prior art are excluded by the recitation of "consisting essentially of," applicant has the burden of showing that the introduction of additional components would materially change the characteristics of applicant's invention. In re De Lajarte, 337 F.2d 870, 143 USPQ 256 (CCPA 1964).

Applicant argues in the affidavit filed August 18, 2005 that DMSO affects the activity of the enzyme, citing the reference by Middleton, by interfering with the activity of enzymes such as trypsin. Applicant's arguments are persuasive; however, this argument is rendered moot in view of the new grounds of rejection as explained supra.

Applicant also argues that the SU1685448 fails to disclose his invention due to the inclusion of the other ingredients, theophylline and lanolin; however,

Applicant has failed to provide any evidence as to why these two ingredients are excluded by use of the term "consisting essentially of". Applicant asserts that lanolin has a potential as an allergen but merely states that his invention does not include an anti-inflammatory agent such as theophylline; however, neither of these statements provide evidence that these ingredients affect the activity of the trypsin. Therefore, the Examiner, in making proper broadest reasonable interpretation of the claims under examination, has concluded that while the phrase "consisting essentially of" excludes the inclusion of DMSO, the phrase is open to the inclusion of theophylline and lanolin.

Applicant's statements directed towards DMSO where Applicant identifies DMSO as an acknowledged penetration enhancer and identifies DMSO as a substance that can cause significant skin irritation are supported by prior art U.S. Patent 5,411,741 to Zaias. The patent, discussing conventional carriers for skin treating compositions delivered to the epidermis (specifically depigmentation agents), teaches against the inclusion of DMSO as a carrier for compositions for treating the skin. At col. 3, lines 5-10, the patent states that DMSO causes extreme skin irritation, redness, itching and scaling. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to practice the method of treating seborrheic keratosis disclosed by SU1685448 by administering a composition containing trypsin but eliminating the DMSO. One of ordinary skill in the art would have been motivated to remove the DMSO since it is known to cause skin irritation. One of ordinary skill in the art would also still have a reasonable expectation of success by using only the trypsin as

the active ingredient because of the disclosure of the other secondary references.

First, per the disclosure of U.S. Patent 4,112,121 to Tenta, conditions such as seborrheic keratosis are known as manifesting a thickening of the outermost (keratinized or hornified) layer of the epidermis to produce beige-colored warty-like areas. These conditions are conventionally treated by a chemoexfoliation or "superficial slough" of the epidermis to peel the outermost skin layer and consequent removal of surface irregularities, blemishes and discolorations. See col. 2, lines 10-50. While Tenta accomplishes this result by use of specific chemical formulation, the physiological effects of superficially sloughing of the seborrheic keratoses while results in the resolution of the condition is pertinent to indicate the level of skill and the knowledge of one of ordinary skill in the art.

Second, per the disclosure of U.S. Patent 5,665,366 to Rawlings et al., trypsin-like enzymes are identified that exist in the stratum corneum and have enzymatic activity similar to trypsin are administered to the skin in the treatment of conditions of the skin where the condition is characterized by hyperkeratinisation, decreased rate of desquamation or where the underlying etiology of the condition indicates that assisting desquamation and/or desmosomal degradation would be beneficial where such enzymes act to degrade the desmosomes (cell-to-cell junctions that hold the skin cells together) and to assist in desquamation (the process of removal of the layers of the skin. See col. 9, lines 25-35. Hyperkeratinisation is a synonym for hyperkeratosis

which is defined as a thickening of the horny layer of the epidermis. Keratoses are defined as lesions on the epidermis marked by the presence of circumscribed overgrowths of the horny layer. As noted by Tenta above, seborrheic keratosis are a form of keratosis. All definitions were obtained from Stedman's Medical Dictionary, 27th edition at http://www.thomsonhc.com/pdrel/librarian/PFDefaultActionId/pdrcommon.Stedmans. The composition may also contain other enzymes, and trypsin is listed as an appropriate enzyme at col. 2, lines 25-45. The amounts of the enzymes may comprise from 0.00001 to 50% of the stratum corneum trypsin-like enzyme and from 0.00001 to 50% of the additional enzyme. At col. 9, lines 49-51, the amount of the composition and frequency of its application depends on the condition of the patient. This reference indicates acknowledgement by those of ordinary skill in the art that enzymes, and particularly trypsin and trypsin-like enzymes, are known to be used to remove layers of epidermis that suffer from certain conditions and particularly those characterized by hyperkeratinization or those conditions that would benefit from desquamation. Per Tenta, one of ordinary skill in the art would understand that seborrheic keratosis is one of these conditions. Therefore, one of ordinary skill in the art would have a reasonable expectation of success in the treatment of seborrheic keratosis with a composition that contains trypsin but eliminates DMSO because one of ordinary skill in the art would expect the trypsin to act on the seborrheic keratotic lesion by degrading the desmosomes and desquamating (i.e. removing) the hyperkeratotic cells of the lesion. When these cells are removed, the lesion is removed and as evidenced

by the disclosures of the prior art, the condition is resolved. It is noted that Rawlings et al. teaches dimethyl sulphoxide (DMSO) as an optional alternative solvent and not a required component of the enzyme composition. See col. 3, lines 23-28.

Finally, Applicant spends an extensive portion of the affidavit filed August 18, 2005 addressing the concept of regulating the removal of the layer of the skin suffering from the condition. This regulation is a function of conventional ezyme kinetics. As evidenced by the discussion of enzyme kinetics at http://web.indstate.edu/thcme/mwking/enzyme-kinetics.html, enzymes are specific for the kind of reaction that they catalyze and, in general, the substrate that they attack. The rate of this reaction is a function of the amount of enzyme, the amount of substrate to be acted upon and the time that the enzyme is permitted to be in contact with the substrate. The greater the enzyme concentration and the longer the exposure time of the enzyme to the substrate, the faster the reaction time and the greater the amount of substrate that is acted upon. Therefore, the disclosure of SU1685448 as to the type and amount of trypsin enzyme as well as the administration procedure does indeed disclose a regulated removal of the layer of the skin that was afflicted by the skin condition by an enzyme in an amount and for a duration effective to treat said condition because the reference teaches the use of the same enzyme as claimed for the treatment of the same condition as claimed and also discloses that upon treatment, the condition was resolved.

In fact, the ability of enzyme having trypsin-like activity to effect removal of some or all of the epidermis is well known per the disclosure of Rawlings et al. Also, the disclosure of Burbach indicates the effect on human skin of proteases, and specifically trypsin, in varying amounts. The conclusion was that trypsin solutions, dependent upon concentration and period of application, were capable of breaking up the connection between the epidermis and the corium (dermis). The reference indicates at page 383 that crystalline trypsin would effect complete detachment of the epidermis after 1-2 hours after injection and disintegration of the epidermis after 3-4 hours after injection

Therefore, the selectivity of trypsin for the epidermal layer as a substrate was well known and the result of topical or injected application of trypsin to the epidermis was known and expected. Therefore the use of a composition consisting essentially of trypsin would have been obvious to one of ordinary skill in the art at the time the invention was made in order to effect a regulated removal of specific areas of the epidermis afflicted by seborrheic keratosis.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jean C. Witz whose telephone number is (571) 272-0927. The examiner can normally be reached on 6:30 a.m. to 4:00 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jean C. Witz
Primary Examiner
Art Unit 1651